REMARKS

This response is being submitted together with an IDS and 16 references, a petition for extension of time for one month for a small entity, and transmittal and fee calculation forms. A check for $235 ($55 for EOT and $180 for IDS) is attached.

In the claims, Claims 1 and 4 are amended, 15 and 16 are withdrawn, 17 is amended, 30-39 are withdrawn and 40 – 48 are added. The total number of claims is still 39, and there are fewer independent claims. The independent claims are now 1, 15 and 40.

All of the claims stand rejected under 35 USC 103(a) as being obvious over Mueller et al. The rejection is respectfully traversed as applied to the claims as amended. Claim 1 as amended now reads:

Claim 1 (amended) A biocompatible tissue-bonding adhesive composition comprising: a polyol of functionality N, wherein said polyol being terminated with at least one polyisocyanate in solution with at least (N-1)% of said solution comprising free polyisocyanate, wherein at least 70% of the polyol is derived from ethylene oxide monomers.

Mueller et al, (US 5,624,972) use mixtures of isocyanate-terminated materials, at least one highly sbstituted (including the starting diisocyanates) and another one less substituted (having a polymer backbone), to make industrial foams. The enabled prepolymers are described in the Glossary (col. 9) and Examples (cols 10 – 12). Where it is stated, the mixtures generally have a predominance of propylene oxide monomers over ethylene oxide, as can be seen in the Glossary, for example for example Polyisocyanate E (col 10 .ine 2), 28% EtO monomer, or Polyisocyanate F (col 10 line line 9), 10% EtO monomer. Based on hydroxyl value, Polymer A is probably in the same range. In the "most preferred" material described in col 8 lines17- 38, preferred compositions have a

polyol having 2 to 30% oxyethylene (lines 22-23) (as is claimed in the European equivalent, EP00442631B1).

These definition of what sorts of materials are of use is the only clear indication of what to practice. Hundreds of polymer types are listed in col 4 line 42 through col 6 line 20, col 6 – col 8, with no indication of which ones might be useful.

Applicants require no more than 30% propylene oxide and at least 70% ethylene oxide. Claim 1 is accordingly amended to require at least 70% ethylene oxide monomer in the polyols used in the invention, This is well supported in the specification, for example at page 15, and pages 19 – 20. As noted above, Mueller et al preferentially use polymers of high propylene oxide content, for example at col. 4 line 63-64. Discussion of polyols and other polymers in Col. 5 focuses on hydrophobic polymers, and for example, in polyether polyamines, only the polypropylene types are even mentioned (col 5 line 51-60.)

In view of Mueller's preferred polymers, and the water content of the final product, applicant's claims as amended are not fairly anticipated, nor would the emphasis on hydrophobic foaming polymers motivate a person to try such compositions as tissue sealants. Should such inspiration be found, the resulting product – application of a hydrophobic product in the process of foaming - would be very unlikely to work. Since Mueller et al would not motivate a person skilled in the art to do what applicants have done, the rejection is respectfully traversed as applied to the claims as amended.

Claims 2-14, being dependent on an allowable independent claim (claim 1), would likewise be allowable.

Claim 15 and dependents 16 – 22 are rejected as obvious over Mueller et al. Claims 15 and 16 are cancelled, and their limitations are incorporated in dependent claim 17. As acknowledged, the composition of claim 17 is not literally found in the reference. However, there is nothing in Mueller that would teach one of ordinary skill how to use Mueller's foaming compositions to form a tissue adhesive. Initial efforts would form a foamy, non-adhering mess, failing to adhere tissue and barring achieving the present composition by "routine experimentation". There being nothing in Mueller to motivate

the formation of a tissue adhesive, thev reference is insufficient and is respectfully traversed.

Claims 23 – 30 are dependent on an independent claim and are likewise allowable if the independent claim is allowable.

NEW CLAIMS

New claims 40 - 48 focus on another difference between the compositions of the invention and the compositions of Mueller et al., which is that applicant's compositions are essentially anhydrous at the time of their application to tissue. The absence of water is prevalent in the application, and water for reaction is derived from the tissue being treated, e.g.at least at page 20, pages 23-24, and pages 27 – 29. The new independent claim is,

Claim 40 (new). A biocompatible tissue-bonding adhesive composition comprising a polyol of functionality N, wherein said polymer being terminated with at least one polyisocyanate in solution with at least (N-1)% of said solution comprising free isocyanate, and wherein said adhesive contains no water at the time of its application to tissue."

As can be seen throughout the specification, applicant's compositions are essentially anhydrous. No water is described as being added to any formulation. Any water that would have been present reacts with the isocyanate in the formulation. The final water for reaction is derived from tissue to which the isocyanate is bonding, as described on pages 23, 27 – 29.

In contrast, Mueller et al use their composition to create a foam, and add water to their composition to make the foam. This feature is found throughout the specification and claims of '972, for example in the abstract; at col 2 line 15, line 28, line 52; in examples 1

– 7; and in claim 1. It seems fair to say that only water-containing final compositions are taught in this reference. There is nothing in Mueller teaching the application of their foams to tissue, nor anything motivating an artisan to do so. Even if there were, the composition of Mueller would already contain water at the time of application. It would be in the process of foaming, and would not adhere to the tissue well, since it would have no particular affinity for the tissue or for its water. In contrast, applicant's anhydrous adhesive reacts preferentially with the tissue and with tissue water, as described.

It is consequently believed that claims 40 – 48 are novel and nonobvious over the Mueller reference, and passage of these claims to allowance is respectfully requested.

It is noted for the record that a response has been made in the corresponding PCT case, PCT/US02/38569, and that no arguments concerning the present reference were made there that are not made here. The three PCT references, which regrettably were not more promptly cited, were US 4,049,5932 and 6,403,269, and the present reference 5,624,972. The former two are cited in the enclosed IDS, and are believed to be less relevant than Mueller. Most of the other IDS references are listed in the specification.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. Applicant's representative is most easily reached at 978-790-7186 if a phone discussion would in any way facilitate prosecution.

Sincerely,

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Reg. 35,219

April 19, 2004